REMARKS

Claims 1-7 are pending, upon entry of the amendment submitted above. Favorable reconsideration is respectfully requested.

The present invention relates to a method for detecting negatively supercoiled DNA in living cells, characterized by including the steps of incorporating biotinylated psoralen into living cells, irradiating the living cells with long-wavelength UV rays, causing the cells to react with adivin which has been labeled with a color-developing substance, a fluorescent substance, or a chemiluminescent substance, and measuring developed color, emitted fluorescence, or emitted chemiluminescence of the cells.. See Claim 1.

The present invention also relates to a method for detecting a living cell containing negatively supercoiled DNA, characterized by including the steps of incorporating biotinylated psoralen into living cells, irradiating the cells with long-wavelength UV rays, causing the cells to react with adivin which has been labeled with a color-developing substance, a fluorescent substance, or a chemiluminescent substance, and measuring developed color, emitted fluorescence, or emitted chemiluminescence of the cells. See Claim 2.

The rejection of the claims under 35 U.S.C. §103(a) over Sinden et al. in view of Saffron et al. and Chevalier et al. is believed to be obviated by the amendment submitted above. The cited references fail to disclose or suggest the claimed methods.

An important feature is that the DNA is detected in living cells. Since the cells are living, the cells are in raw state and not frozen or fixed.

Sinden et al. teach that measurement of supercoiled DNA using biotinylated psoralen. Although this reference describes a method of measuring supercoiled DNA, the method described therein requires electrophoretic separation. Sinden et al. fail to describe detecting negatively supercoiled DNA in living cells as claimed.

Saffran et al. teach a method of cross-linking biotinylated psoralen to DNA. However, this method requires that hybridization be carried out after DNA has been isolated.

Chevalier et al. describe in situ hybridization using biotin and avidin. However, biotinylation in such a procedure is performed using frozen or fixed tissue, preferably fixed and embedded tissue (see p. 483, right column, lines 6-11; p. 484, left column, lines 5-14; p. 488, left column, line 9 from the bottom to line 4 right column), rather than a raw, unfixed tissue as specified in the claimed methods.

Moreover, this reference describes that digoxigenin is more preferable for labeling that biotin since biotin has some disadvantages for use in situ (see p. 482, left column, line 9 from the bottom to right column, line 4). Thus, those skilled in the art would not be motivated to use biotin-avidin in raw tissue as claimed.

In addition, with the present invention, negative supercoils of DNA can be detected in whole genome in simple manner, in contrast to conventional methods which require complex procedures to detect the coils at limited portions in the genome.

Indeed, the method thus accomplished by the present invention is bringing many benefits to this medical field. For instance, it has become possible to discriminate between human leukemia cells and leukocytes, thanks to the method of the present invention. The Rule 132 Declaration of Dr. Hirose submitted on December 21, 2007 discusses that striking result.

Moreover, prior to the present invention, it had been conjectured that psoralen signals would be detected in only several regions of the genome because negative supercoils had been detected in only two regions of the genome using a conventional method. However, according to the present invention, many psoralen signals were unexpectedly observed in chromosomes, which is another unexpected effect of the invention.

In view of the foregoing, the claimed methods specified are not obvious over Sinden et al. in view of Saffron et al. and Chevalier et al. Accordingly, withdrawal of this ground of rejection is respectfully requested.

Claim 7 further distinguishes that claimed method from the cited references.

As discussed in the specification, the present invention is the first method to visualize negatively supercoiled DNA on interphase chromosomes. See the Examples in the specification and, in particular, page 21, lines 3-5. That significant feature is recited in Claim 7.

Sinden et al. describe a method for assaying DNA supercoiling and topological domain size using trimethyl psoralen (see the Abstract and Table 1 at page 116). Saffran et al. describe biotinylated psoralens (see the Abstract). Chevalier et al. reviews the use of biotin and digoxigenin as labels for hybridization probes.

None of the cited references describe detecting negatively supercoiled DNA on interphase chromosomes. In fact, each of Sinden et al., Saffran et al. and Chevalier et al. are completely silent about interphase chromosomes.

In fact, as discussed in the specification, the present invention provides the first method for detecting negatively supercoiled DNA in interphase chromosomes. Sinden et al., Saffran et al. and Chevalier et al., taken in combination, fail to suggest that important feature. Accordingly, the method recited in Claim 7 is certainly not obvious over Sinden et al. in view of Saffron et al. and Chevalier et al.

Applicants submit that the present application is in condition for allowance. Early notice to this effect is earnestly solicited.

Respectfully submitted,

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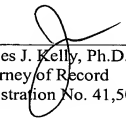

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